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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,101	07/08/2003	Ying Luo	RIGL-010CIP3	5361

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EXAMINER	
RAO, MANJUNATH N	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/616,101	LUO ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-47* is/are pending in the application.

4a) Of the above claim(s) *45-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/03,10/04,3/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 38-47 are currently pending and are present for examination. Claims 38-44 are now under consideration. Claims 45-47 remain withdrawn from consideration being drawn to non-elected invention.

Election/Restrictions

Newly submitted claims 45-47 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Inventions I of claims 38-44 and Invention II of claims 44-47 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the composition comprising a recombinant tankyrase H protein can be used to raise specific antibodies as opposed to its use in the method of claims 45-47.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 44-47 have been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicant's election with traverse of Group VII, which read on current claims 38-44 in Paper filed on 3-17-06 is acknowledged. The traversal is on the ground(s) that claims 44-47 represent a method of using the subject matter of claim 38 and therefore should not be restricted and that it would not be unduly burdensome to perform a search on all of the claims together in

the application. This is not found persuasive because while the searches for the two groups may overlap, they are not coextensive. The search for the two above Groups would each require the search of subclasses unnecessary for the search of elected Group.

The requirement is still deemed proper and is therefore made FINAL.

Claims 44-47 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper filed on 3-17-06.

Rejoinder of restricted inventions

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. **Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112.** Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. **Withdrawn process claims that are not commensurate in scope with an**

allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to rejoin, in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Specification

The disclosure is objected to because of the following informalities: Examiner notes that applicants have not updated the relationship of the instant application to its parent application that has matured in to a US patent in the 1st line of the specification. Examiner urges applicants to amend said information by providing the US patent number in response to this Office action. Appropriate correction is required.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence

identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that applicant fails to provide the appropriate SEQ ID NOs to sequences recited in the specification, for example at pages 14, 44, 45, 61 and in Figures 8 and 16. See particularly 37 CFR 1.821(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 38 recites the phrase "wherein said composition exhibits poly-ADP ribose polymerase activity". While the composition comprises a recombinant Tankyrase H protein, it is not clear to the Examiner whether it is the composition that comprises substances other than the recombinant polypeptide that exhibits the above activity or whether it is the recombinant Tankyrase H that exhibits the above activity. Examiner requests clarification.

Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 39 recites the phrase "a test agent". The metes and bounds of the above phrase is not clear to the Examiner. It is not clear as to what all agents are encompassed in the above phrase. A perusal of the specification did not provide the Examiner with a clear definition for the above phrase. Examiner requests clarification.

Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 44 recites the limitation "said cell is a mammalian cell" in line 1. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 38-44 are drawn to a "non-naturally occurring composition comprising a Tankyrase H protein, further comprising a test agent, wherein said test agent is an organic molecule of less than 2500 Da and wherein said Tankyrase protein can also be a fusion protein". However, a perusal of the specification indicates that applicants have no support for "non-naturally occurring composition" and "a test agent" which now constitutes a "new matter". A perusal of the specification did not provide the Examiner with any support for the above two phrases and applicants also fail to point out the support for the amended claims. Therefore claims 38-44 are rejected for introducing "new matter" into the claims.

Claims 38-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising the amino acid sequence of SEQ ID NO:3 or

4 or a fusion protein comprising SEQ ID NO:3 or 4 fused to GFP and a known test agent and as a source of ADP ribose, does not reasonably provide enablement for a composition comprising any Tankyrase H protein or a fusion protein of the same (i.e., any variant or mutant or recombinant including variants and mutants of SEQ ID NO:3 or 4 isolated from any or all sources) comprising any substance as a test agent and source of ADP-ribose. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 38-44 are so broad as to encompass any Tankyrase H protein or a fusion protein of the same (i.e., any variant or mutant or recombinant including variants and mutants of SEQ ID NO:3 or 4 isolated from any or all sources) comprising any substance as a test agent and source of ADP-ribose. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of Tankyrase H proteins, test agents and source of ADP-ribose broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence to obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any,

are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of only two Tankyrase H polypeptides, SEQ ID NO:3 or 4. It would require undue experimentation of the skilled artisan to make and use the composition comprising the claimed polypeptides. The specification is limited to teaching the use of SEQ ID NO: 3 or 4 as a Tankyrase H in a composition, but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass a composition comprising all modifications and fragments of any Tankyrase H, any test agent and any source of ADP-ribose because the specification does not establish: (A) regions of the protein Tankyrase H protein structure which may be modified without affecting its activity; (B) the general tolerance of Tankyrase H to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; (D) specific class of compounds contemplated as test agents; (E) a specific list of sources of ADP-ribose that can be used in the composition; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including Tankyrase H with an enormous number of amino acid modifications SEQ ID NOS:3 or 4. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of compositions comprising Tankyrase H having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 38-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 38-44 are directed to composition comprising a recombinant Tankyrase H protein, a source of ADP-ribose and test agent. Claims 38-44 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides having poly-ADP ribose polymerase activity including mutants, variants and recombinants (i.e., modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue in SEQ ID NO:3 or 4) that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of SEQ ID NO:3 or 4 has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the structure of all the polypeptide sequences derived from SEQ ID NO:3 or 4, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including those which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed. Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 38-40, 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Simonin et al. (J. Biol. Sci., Vol. 268(12):8529-35, 1993). This rejection is based upon the public availability of a printed publication. Claims 38-40, 42 of the instant application are drawn to a composition comprising a recombinant Tankyrase H, a source ADP –ribose wherein said enzyme has ADP-ribose polymerase activity, wherein said composition comprises a test agent such as a organic molecule of less than 2500 Da and wherein said composition is a cellular composition expressing the recombinant tankyrase. Simonin et al. disclose such a composition comprising a recombinant Tankyrase H, a source ADP –ribose wherein said enzyme has ADP-ribose polymerase activity, wherein said composition comprises a test agent such as a organic molecule of less than 2500 Da (see page 8530, column 2, 4th paragraph). The reference also discloses a E.coli cell preparation expressing the recombinant tankyrase having the poly-ADP ribose polymerase activity. Thus Simonin et al. anticipate claims 38-40, 42 of this application as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 41, 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simonin et al. as applied to claims 38-40, 42 above, and further in view of Smith et al. (Science, Vol. 282, pages 1484-1486, 1998) and the common knowledge in the art regarding mammalian cellular assay and making fusion proteins. Claims 41, 43-44 are drawn to a composition comprising a recombinant Tankyrase H, a source ADP –ribose wherein said enzyme has ADP-ribose polymerase activity, wherein said composition comprises a test agent such as a peptide and wherein said composition is a mammalian cellular composition and the tankyrase H is a fusion protein.

The reference of Simonin which teaches a composition comprising a recombinant Tankyrase H, a source ADP –ribose, wherein said enzyme has ADP-ribose polymerase activity, and wherein said composition is a cellular composition which comprises a test agent such as a small organic molecule has already been discussed above. However, the reference does not teach a test agent which is a peptide or a composition comprising a mammalian cell encoding a recombinant tankyrase H protein or that the tankyrase H protein is a fusion protein.

Smith et al. teach that tankyrase is a Poly (ADP-ribose) polymerase found at human telomeres and that it binds to TRF1 a negative regulator of telomere length. The reference also teaches a method of making histidine tagged tankyrase fusion protein and transfection of the same to insect cells.

With the teachings of the above two references in hand, it would have been obvious to one of ordinary skill in the art to arrive at a mammalian cell composition expressing the

recombinant tankyrase as a His-tagged fusion protein. One of ordinary skill in the art would have been motivated to do so in view the teaching of Smith et al. that tankyrase regulates the telomere length in mammalian cells. Therefore one of ordinary skill in the art would make the vector expressing the recombinant fusion protein as taught by Smith and express the same in a mammalian cell such as a HeLa cell in order to study the specific role of tankyrase in cell growth. On similar lines, one of ordinary skill in the art would have been motivated to use random peptides as test agents because it is well known in the art that peptides can bind to enzymes and regulate it s activity. One of ordinary skill in the art would have a reasonable expectation of success because Smith et al. teach that tankyrase is a protein that is normally expressed in the mammalian protein and also demonstrate the making of fusion protein that can be expressed in an insect cell which technique could be applied to any mammalian cell.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

May 23, 2006